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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/727,084	10/08/96	PULST S	P07-37217

18N2/1203
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EXAMINER	
ALLEN, M	
ART UNIT	**PAPER NUMBER**
1817	19

DATE MAILED: 12/03/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

See the attached.

PTO-90C (Rev. 2/95)
*U.S. GPO: 1997-422-198/60031

1- File Copy

Office Action Summary	Application No. 08/727,084	Applicant(s) Pulst et al.
	Examiner Marianne Allen	Group Art Unit 1817

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-15, 37, 40, and 43-54* is/are pending in the application.

Of the above, claim(s) *15, 37, 44-48, 50, and 51* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-14, 40, 43, 49, and 52-54* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-15, 37, 40, and 43-54* are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 6

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1817.

Claims 16-36, 38-39, and 41-42 have been cancelled. Claims 44-54 have been newly added.

Applicant's election of Group I with traverse as to Groups II and IX in Paper No. 14 is acknowledged. The traversal is on the ground(s) that no burden of search or different classification existed between Groups I and (II and IX). This is not found persuasive because Group I is classified in Class 536, subclass 23.5 and Group II is classified in Class 536, subclass 24.5 thereby establishing different classification and burden of search. The classification for Group IX was inadvertently omitted in the prior Office action; however, such methods of diagnosis are classified in Class 435, subclass 6 and/or Class 536, subclasses 24.3 and 24.33. Again, different classification and burden of search exists between Group I and Group IX.

The requirement is still deemed proper and is therefore made FINAL.

Claims 15, 37, 44-48, and 50-51 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 14.

Claims 1-14, 40, 43, 49, and 52-54 are under consideration by the examiner.

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The specification does not claim priority to the provisional applications nor acknowledge the duty to disclose to the Office all information known to the person to be material to patentability as defined in 37 CFR 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

The disclosure is objected to because of the following informalities:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with one or more of the requirements of 37 CFR § 1.821 through 1.825.

It is noted that the sequences disclosed on pages 43, 45, 46, and 47 and in Figure 7 are not present in the sequence listing.

It is noted that any corrections to the sequence listing will require submission of a new CRF. A new sequence listing will need to be submitted to replace the present one in the specification. A statement that the content of the paper and computer readable copies are the

same and contain no new matter would also need to be submitted. Appropriate correction is required. Applicant must direct entry of the new sequence listing to replace the old one in the specification and must reference all sequence identifiers appropriately in the specification.

Appropriate correction is required.

Claims 1-14, 40, 43, 49, and 52-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and/or are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification discloses SEQ ID NO: 2 (4481 base pairs) which corresponds to the nucleic acids sequence encoding the human species of the SCA2 protein (1312 amino acids), SEQ ID NO: 3. This SEQ ID NO. meets the written description provision of 35 USC 112, first paragraph. SEQ ID NO: 1 is a partial human genomic sequence (516 base pairs) and SEQ ID NO: 4 is a partial mouse cDNA (1257 base pairs) encoding SEQ ID NO: 5 (418 amino acids). However, the claims are directed to or encompass sequences that hybridize to mammalian SCA2 polypeptides from other species, mutated sequences, allelic variants, splice variants, sequences

that are "substantially the same"and so forth. None of these sequences meets the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 2 and degenerate sequences which encode SEQ ID NO: 3, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides or proteins and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, the only SEQ ID NO: 2 and degenerate sequences encoding SEQ ID NO: 3 but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

See also the July 22, 1997, CAFC decision of The Regents of the University of California v. Eli Lilly and Company where generic claims to vertebrate and mammalian insulin cDNA's were found to be invalid because of lack of adequate written description where only the rat sequence was disclosed.

The partial sequences of SEQ ID NOS: 1, 4, and 5 are not of sufficient size or similarity to permit one to visualize the complete sequence for the SCA2 polypeptides nor nucleic acid sequences encoding them. It is noted that the specification itself indicates that the mouse and the human SCA2 sequences have only a short region of high homology and that the gene product ataxin-2 has significant similarity to a domain of an unrelated protein, A2RP.

It is noted that the specification identifies no known biological activity for the SCA2 polypeptide or ataxin-2 (it is unclear if these terms are interchangeable) and provides no assays for determining such. As the definition on page 15 for SCA2 polypeptide requires biological activity, the alternate forms included within the SCA2 definition are not enabled.

In addition, claim 6 recites "substantially the same." This phrase is discussed on page 11 of the specification; however, insufficient details are provided to permit one to determine the

metes and bounds of sequences encompassed. That is, no particular hybridization conditions are provided nor any algorithm to determine degree of homology.

In addition, claim 5 recites "hybridizes under high stringency conditions." Hybridization is discussed on pages 13 and 20 of the specification; however, insufficient details are provided to permit one to determine the metes of bounds of conditions (and therefore the sequences) the claims encompass.

The specification does not appear to set forth how to use the oligonucleotide composition of claim 14. Clarification is requested.

Claims 8-9 recite a "host cell" which encompasses transgenic animals. These are not enabled by the specification. It would not have been so predictable to be able to produce such an animal and the specification does not appear to set forth any particular use for such an animal. This portion of the rejection could be obviated by amending the claims to refer to an "isolated host cell."

Claim 12 is directed to a kit for detecting mutations at the SCA2 locus in 12q24.1. The only mutation at this locus disclosed is a change in the number CAG repeats. As such, only those subsequences of SEQ ID NO: 2 that could be used to directly hybridize to these repeats or that could be used as primers to amplify this region would be capable of detecting these mutations. The same is true with respect to claim 40.

Claims 4-5, 12, 40, 43, 49, and 52-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is confusing in its dependency upon claim 2. Claim 4 recites "encodes at least about 10 contiguous amino acids." Such a sequence would not possess all of the limitations of claim 2 which is required to encode a SCA2 polypeptide (a full length protein with biological activity). It appears that this claim is not properly dependent or at least is confusing as to what is being claimed.

Claim 5 is confusing in its dependency upon claim 2. Claim 5 recites "hybridizes under high stringency conditions." Such a sequence would not necessarily possess all of the limitations of claim 2 which is required to encode a SCA2 polypeptide (a full length protein with biological activity). It appears that this claim is not properly dependent or at least is confusing as to what is being claimed.

Claim 12 is confusing in reciting "for detecting mutation and in chromosome 12." It appears that "and" should be deleted or there is a word missing.

Claim 40 is confusing in reciting "diagnosis of SCA2." It appears that the claim is intended to mean detecting the number of CAG repeats in the disease versus normal state for the SCA2 locus; however, the claim does not make this clear. The specification does not appear to indicate that the term "SCA2" is only referring to the disease state.

Claim 43 is incomplete in reciting "diagnostic kit" and failing to indicate what is being diagnosed.

Claim 49 is directed to the DNA produced by the method of claim 46. This claim is confusing because claim 46 is directed to a method and it does not produce a DNA fragment. The fragment is merely detected not produced or isolated. Furthermore, the claim depends upon a non-elected claim.

Claim 52 is confusing in reciting a sequence "comprising bases 631-648...of SEQ ID NO: 2...and a CAG repeat region." Bases 631-648 of SEQ ID NO: 2 are not contiguous with the CAG repeat region. The CAG repeat region begins at base 658. This claim fails to indicate how the named nucleotide range and the CAG repeat region are connected or related to each other. That is, the claim could be interpreted as having a CAG repeat region upstream of bases 631-648. This claim could be considered new matter. Applicant is cautioned against introducing new matter when amending the claim to clarify what is being claimed.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Applicant is being given benefit to only the instant filing date, namely 10/8/96, as neither of the provisional applications disclose the nucleic acid sequences found in the instant application.

Claims 1-4, 10, 12, 13, and 40 are rejected under 35 U.S.C. 102(a) as being anticipated by EST Accession No. W39162 from the WashU-Merck EST Project.

This EST has 417 nucleotides of which 393 match SEQ ID NO: 2. It encodes the last 9 amino acids of SEQ ID NO: 3. "At least about 10" in claim 4 is interpreted to include 9 amino acids in the absence of a specific definition. Absent evidence to the contrary, this fragment is deemed to encode a protein that meets the definition of a SCA2 polypeptide. The functional language "for detecting..." and "for amplification diagnosis..." is given no patentable weight in the product claims of claims 12 and 40. The EST meets all of the structural requirements of claims 12 and 40. With respect to claim 13, the EST information indicates that it originated as an mRNA from sporadic parathyroid adenomas.

Claims 5, 10-12, 40, 43, and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Orr et al.

Orr et al. discloses a 400 bp fragment with CAG trinucleotide repeats. $(GCT)_7$ PCR primers were used as a CAG repeat probe. This primer could also be labelled with P^{32}. (See page 225.) This primer would hybridize to the recited sequences. The functional language "for detecting..." and "for amplification diagnosis..." is given no patentable weight in the product

claims of claims 12 and 40. The primer meets all of the structural requirements of claims 12 and 40. With respect to claim 43, the primer would have been made and stored in some sort of container thereby meeting the limitation of "packaging material."

Claims 5, 10-12, 40, 43, and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawaguchi et al.

Kawagūchi et al. discloses a probe for detecting CAG trinucleotide repeats. The $GATCT(CTG)_{13}G$ was used as a CAG repeat probe. This probe was labelled with P^{32}. (See page 226.) This primer would hybridize to the recited sequences. The functional language "for detecting..." and "for amplification diagnosis..." is given no patentable weight in the product claims of claims 12 and 40. The probe meets all of the structural requirements of claims 12 and 40. With respect to claim 43, the primer would have been made and stored in some sort of container thereby meeting the limitation of "packaging material."

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Navot et al. (U.S. Patent No. 5,650,277) discloses methods of quantifying di- and trinucleotide repeats. The CAG repeats of Huntington's Disease and SCA1 are disclosed. (See abstract, claims, Figure 3, and columns 3 and 18.)

Giese et al. (U.S. Patent No. 5,650,270) discloses a polyglutamine polymer. (See Table IV at column 15.)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen, whose telephone number is (703) 308-0666. The examiner can normally be reached on Monday-Friday from 6:30 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, Ph.D., can be reached on (703) 308-4310. Official FAX communications may be directed to either (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
GROUP 1800